Tetrahedron: *Asymmetry* 20 (2009) 1185–1190

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Chiral (salen)Co(III)(*N*-benzyl-L-serine)-derived phosphites: monodentate P-ligands for enantioselective catalytic applications

Stefano Carboni [a], Luca Pignataro [a,b], Cesare Gennari [b,*], Umberto Piarulli [a,*]

[a] *Dipartimento di Scienze Chimiche e Ambientali, Università degli Studi dell'Insubria, Via Valleggio 11, Como I-22100, Italy*
[b] *Dipartimento di Chimica Organica e Industriale, Centro Interdipartimentale C.I.S.I., Università degli Studi di Milano, Via Venezian 21, Milano I-20133, Italy*

ARTICLE INFO

Article history:
Received 3 March 2009
Accepted 1 April 2009
Available online 6 May 2009

ABSTRACT

Reaction of the (*S,S*)-salen-cobalt(III)-*N*-benzyl-L-serine complex **2** with four diol-derived chlorophosphites afforded phosphites **3a–3d** in moderate yields (37–72%). Structural studies of these monodentate phosphite ligands and of their Rh-complexes were performed in solution by ^{1}H and ^{31}P NMR spectroscopy. The ligands were screened in several enantioselective catalytic applications, showing good activity and moderate enantioselectivity in the palladium-catalyzed desymmetrization of *meso*-cyclopenten-2-ene-1,4-diol biscarbamate.

1. Introduction

Chiral (salen)cobalt(II) and cobalt(III) complexes have found wide application in several asymmetric transformations.[1] We have recently reported a novel approach to the resolution of racemic *N*-benzyl α-amino acids (*N*-Bn-AA) by liquid–liquid extraction, using the lipophilic chiral (salen)cobalt(III) complex (*R,R*)-*N,N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclo-hexanediaminocobalt(III) acetate, in excellent yield and enantioselectivity.[2] As a result of the resolution by extraction, one enantiomer of the *N*-benzyl α-amino acid predominates in the aqueous phase, while the other enantiomer is driven into the organic phase by complexation to the cobalt center. The complexed amino acid can then be released by a reductive ($Co^{III} \rightarrow Co^{II}$) counter extraction into an aqueous phase. The original chiral cobalt(III) complex can be regenerated and reused with essentially no loss of reactivity and selectivity. Spectroscopic and molecular modeling investigations have revealed that, in the (*N*-Bn-AA)Co(salen) complex the (*R,R*)-salen ligand is in a cis-β-folded arrangement around the octahedral cobalt ion, with the remaining two cis coordination sites being occupied by the *N*-benzylamino acid.[2b] The amino acid coordination takes place in such a way that a meridional arrangement of the three oxygen and three nitrogen atoms is obtained (meridional N_3O_3 structure). Using the (*R,R*)-salen ligand, the favored diastereomeric complex contains the (*R*)-enantiomer of the *N*-benzylamino acid, while the absolute configuration of the additional stereogenic elements (the octahedral cobalt and the tetrasubstituted nitrogen of the *N*-benzylamino acid) was assigned as Δ and (*S*), respectively. As a consequence, the *N*-benzylamino acid is nicely accommodated in the binding pocket of the chiral cobalt complex.

Prompted by these achievements, we decided to take advantage of the (salen)cobalt(III)-*N*-Bn-AA coordination properties and to develop a salen-cobalt(III)-*N*-benzyl-serine complex as a chiral platform for the preparation of new families of monodentate P-ligands (Fig. 1).

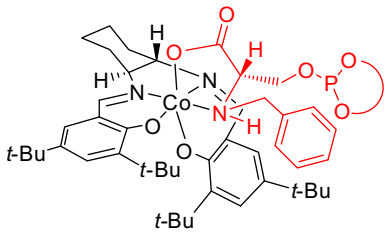


Figure 1. Monodentate (salen)cobalt(III)(*N*-Bn-Ser) phosphites.

Herein we report the synthesis of several phosphites obtained by reaction of the (*S,S*)-salen-cobalt(III)-*N*-benzyl-L-serine complex with diol-derived chlorophosphites and their application to Pd-catalyzed allylic substitution reactions.

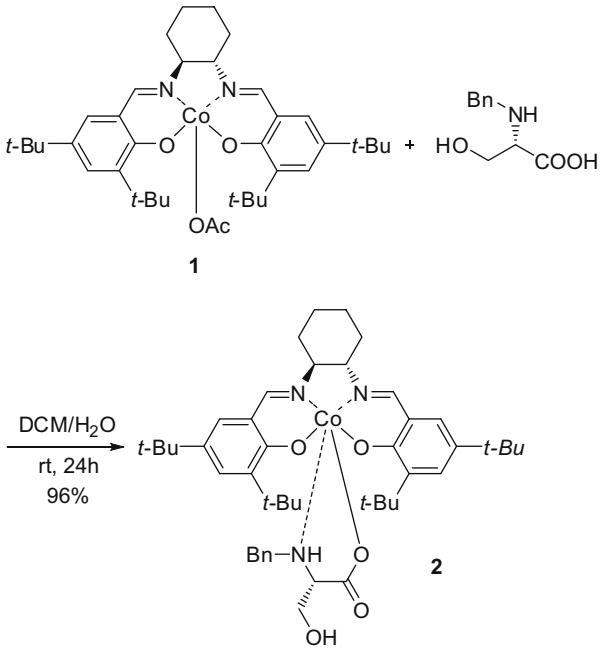
2. Results and discussion

2.1. Synthesis of the ligands

The chiral (salen)cobalt(III) acetate complex **1** was prepared following well-established procedures,[3] starting from commercially available (*S,S*)-*N,N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclo-hexanediaminocobalt(II). (*S,S*)-Salen-cobalt(III)-*N*-benzyl-L-serine complex **2** was then easily synthesized (Scheme 1), applying our

* Corresponding authors. Tel.: +39 02 5031 4091; fax: +39 02 5031 4072 (C.G.); tel.: +39 031 238 6444; fax: +39 031 238 6449 (U.P.).
E-mail addresses: cesare.gennari@unimi.it (C. Gennari), umberto.piarulli@uninsubria.it (U. Piarulli).

0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.04.001



Scheme 1. Synthesis of the (*S,S*)-salen-cobalt(III)-*N*-benzyl-L-serine complex **2**.

reported biphasic extraction procedure,[2a,b] starting from (*S,S*)-**1** and using 2 equiv of *N*-benzyl-L-serine.

The biphasic procedure, where the water-soluble *N*-benzyl-L-serine is extracted into the dichloromethane phase, following complexation to the cobalt center, was preferred to reaction in pure dichloromethane, where *N*-benzyl-L-serine is sparingly soluble and the complexation becomes extremely slow. The reaction was performed on a multigram scale and complex **2** was obtained in excellent yield (96%) after chromatographic purification over silica gel, thus confirming the excellent stability of these complexes.

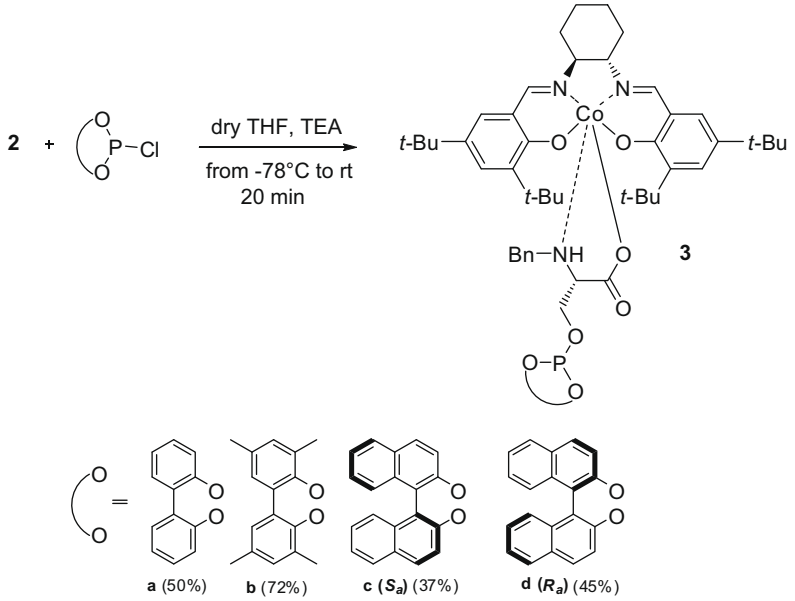
The corresponding phosphite ligands **3a–3d** were then synthesized by reaction of complex **2** with four (*tropos* and *atropos*) diol-derived chlorophosphites.[4] The chlorophosphites were added at low temperature and the reaction mixtures were then warmed to room temperature and stirred for 20 min. After purification by flash chromatography, phosphites **3a–3d** were obtained in moderate yields (37–72%, Scheme 2).

We found that longer reaction times were not beneficial to the yields and, on the contrary, caused decomposition of the product. In the synthesis of **3a,** a decomposition product was isolated and tentatively characterized as a cobalt(III) complex containing the chiral salen moiety, a biphenyl phosphorous acid diester ligand, and no trace of the *N*-benzylamino acid. The structure of the ligand was supported by the ^{31}P NMR spectrum where a singlet at δ 37.5 ppm was detected.[5] Chiral phosphorous acid diesters, which exist in a tautomeric equilibrium between a $(RO)_2P–OH$ and a $(RO)_2(H)P{=}O$ form, have recently been reported to perform as active and enantioselective ligands in the Ir-catalyzed hydrogenation of imines.[5] From a mechanistic point of view, it can be assumed that, once formed, the phosphite activates the OH group of the serine toward an elimination reaction, which is promoted by the base (TEA) present in the reaction medium. The biphenyl phosphorous acid diester which is thus formed, apparently acts as a better ligand toward cobalt and displaces the amino acid derivative.

An analogous synthetic pathway was attempted using *N*-benzyl-L-threonine instead of serine to study the effect of an additional stereogenic center. The chiral (*S,S*)-salen-cobalt(III)-*N*-benzyl-L-threonine complex was prepared and isolated, after flash chromatography, in good yield (83%).[2b] Unfortunately, all attempts to proceed further with the formation of the phosphite met with no success and only the decomposition complex described above could be isolated.

2.2. Structural and complexation studies

A NMR investigation of the ligands was then undertaken. The experiments were conducted in $CDCl_3$, which was degassed and passed over a short pad of neutral alumina. ^{1}H NMR NOESY studies, performed on ligand **3a**, showed a number of common contacts to the parent (salen)cobalt(III)-*N*-benzyl-L-serine, thus revealing a similar configuration of the octahedral cobalt ion and arrangement of the substituents.[2b] The ^{31}P NMR spectra of the phosphites displayed a singlet at similar chemical shifts in all cases: **3a**, δ 144.6 ppm; **3b**, δ 150.7 ppm; **3c**, δ 146.6 ppm; **3d**, δ 144.2 ppm.



Scheme 2. Synthesis of the (*S,S*)-salen-cobalt(III)-*N*-Bn-L-serine-derived phosphites **3a–d**.

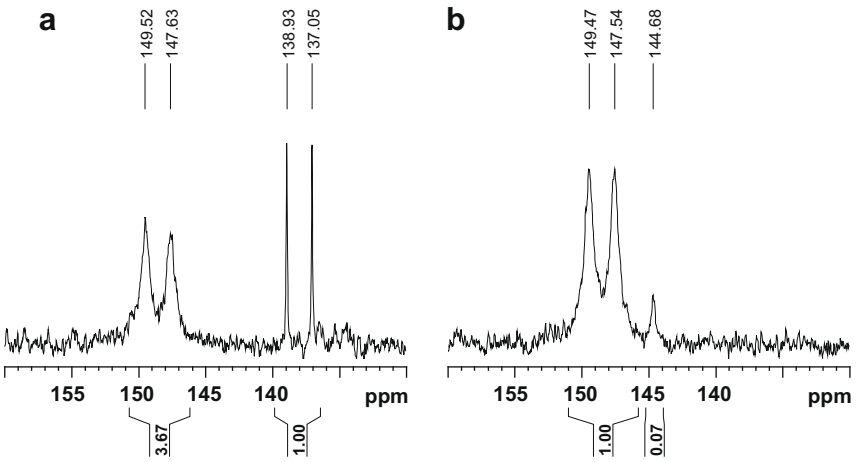


Figure 2. ^{31}P NMR spectra of the rhodium complexes resulting from the combination of ligand **3a** with $Rh(acac)(C_2H_4)_2$ in (a) 1:1 ratio and (b) 2.1:1 ratio.

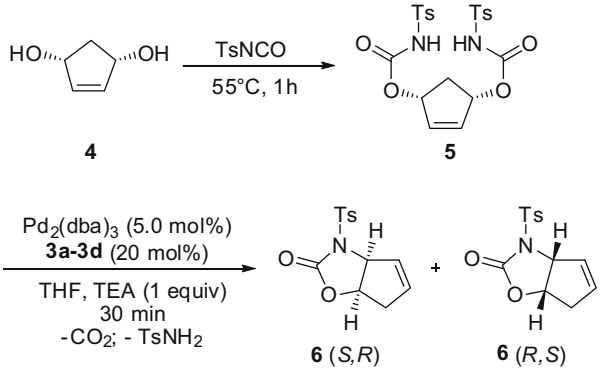
The complexation of ligand **3a** with $[Rh(acac)(C_2H_4)_2]$ was then studied (Fig. 2). Upon addition of 1.0 equiv of **3a** with respect to the rhodium source, a doublet at δ 148.6 ppm (J_{P-Rh} = 312.2 Hz) and a doublet at δ 138.0 ppm (J_{P-Rh} = 302.2 Hz) were observed (in 3:1 ratio). When the ratio **3a**/Rh was increased to 2.1:1, the spectrum displayed only the doublet at δ 148.6 ppm, plus a small singlet at δ 144.6 ppm corresponding to excess ligand. Therefore, it can be concluded that the doublet at δ 138.0 ppm corresponds to the substitution of one ethylene molecule, while the doublet at δ 148.6 ppm contains two ligands coordinated to the rhodium atom. It is interesting to note that two ligands are accommodated around the rhodium atom, notwithstanding their steric hindrance.

2.3. Catalytic applications

The ligands were then screened for several enantioselective catalytic applications. Unfortunately, in the rhodium-catalyzed enantioselective hydrogenation of functionalized olefins and in the rhodium-catalyzed asymmetric conjugate addition of arylboronic acids to enones, reduction of cobalt(III) to cobalt(II) was observed, with consequent loss of the (salen)Co(*N*-Bn-Ser) phosphite ligand integrity. On the contrary, when the Pd-catalyzed allylic substitution of *rac*-1,3-diphenyl-3-acetoxyprop-1-ene with dimethyl malonate was tested,[6] the ligands proved to be perfectly stable and gave excellent conversions, albeit with low enantiomeric excess (up to 35% ee using ligand **3a**). Quite surprisingly, the use of bulkier 3,3′,5,5′-tetramethyl-2,2′-biphenol derivative **3b** gave the opposite enantiomer, while the use of axially chiral BINOL derivatives **3c** and **3d** led to racemic products.

Ligands **3a–3d** were then screened in the Pd-catalyzed desymmetrization of *meso*-cyclopenten-2-ene-1,4-diol biscarbamate **5** (Scheme 3).[7] This intramolecular allylic substitution reaction was developed by Trost and co-workers and has proven to be a very powerful method in several synthetic approaches to biologically relevant targets.[8] The ligands used in the original examples are chiral bidentate phosphines and give the product with excellent enantioselectivity (ee up to 99%)[9] while, to our knowledge, no monodentate phosphite ligands have ever been reported for this reaction.

The reaction was performed using 10 mol % of palladium (5% of the dimer Pd_2dba_3) and 20 mol % of ligands **3a**–**3d**. In several cases, a stoichiometric amount of triethylamine (TEA), which has been reported to increase the enantioselectivity of the reaction,[9] was added to the mixture. The results are summarized in Table 1.



Scheme 3. Pd-catalyzed desymmetrization of *meso*-cyclopenten-2-ene-1,4-diol biscarbamate.

Table 1
Screening of ligands **3a**–**3d** in the Pd-catalyzed desymmetrization of *meso*-cyclopenten-2-ene-1,4-diol biscarbamate **5**

Entry	Ligand	T (°C)	TEA	Conv. (%)[a]	**6** (*S,R*):(*R,S*)[b]
1	None	25	No	—	—
2	**3a**	25	No	96	50:50
3	**3a**	25	Yes	100	15:85
4	**3a**	0	Yes	85	18:82
5	**3b**	25	Yes	90	48:52
6	**3b**	0	Yes	90	28:72
7	**3c**	25	No	100	90:10
8	**3c**	25	Yes	99	80:20
9	**3d**	25	No	100	35:65
10	**3d**	25	Yes	93	32:68

[a] Determined by ^1H NMR analysis of the crude reaction mixture.
[b] er values and absolute configurations were determined by HPLC using a Chiralcel OD-H column (see Ref. 9).

Reaction conversions were always good, in many cases quantitative, with all four ligands **3a**–**3d**. Addition of TEA to the reaction with ligand **3a** was fundamental to achieve higher levels of enantioselectivity while, in the case of ligand **3c**, TEA had a negative effect. Remarkably, the use of complex **3a**, containing a *tropos* biphenol moiety (entries 3 and 4), afforded enantiomeric ratios comparable (yet opposite) to **3c**, containing an *atropos* (S_a)-1,1′-binaphthyl moiety (entries 7 and 8). All these observations confirm that the chiral and well-organized structure of the salen-cobal-

t(III)-*N*-benzyl-L-serine complex is relevant in determining the stereochemical outcome of the reaction.

3. Conclusion

In this work, we have investigated the use of an octahedral (*S*,*S*)-(salen)cobalt(III)-*N*-benzyl-L-serine complex for the formation of monodentate phosphites, to be used as chiral ligands in enantioselective catalytic applications. The ligands were obtained in moderate yields by reaction of (*S*,*S*)-(salen)cobalt(III)-*N*-benzyl-L-serine with diol-derived chlorophosphites. These phosphites showed remarkable air and moisture stability. ^{1}H NMR NOESY studies revealed that formation of the phosphite does not alter the original structure of the (salen)cobalt(III)-*N*-Bn-L-serine complex.[2b] These ligands were then screened for several asymmetric catalytic applications, showing good activity and moderate enantioselectivity in the palladium-catalyzed desymmetrization of *meso*-cyclopenten-2-ene-1,4-diol biscarbamate.

Coordination complexes have recently been used for the preparation of supramolecular bidentate P-ligands.[10] In this approach, two monodentate P-ligands self-assemble around a transition metal (Rh, Pd) by virtue of an additional coordinative bonding of nitrogen to zinc. In particular, Reek and co-workers developed a 'SUPRAPhos' library, where the supramolecular bidentate P-ligands are formed by a porphyrinatozinc(II)···pyridyl interaction.[11] The members of this library include porphyrin phosphites and phosphoramidites, pyridyl phosphites, phosphoramidites and phosphanes. Using a different approach, Takacs and co-workers reported the use of enantiomeric chiral bisoxazolines to direct the self-assembly upon addition of zinc(II), with preferential formation of the heterodimeric zinc(II)-complexes.[12] The bifunctional chiral bisoxazolines were substituted with a series of phenylmethyl or biphenylmethyl tethers terminating in a TADDOL-derived phosphite. The advantage of these supramolecular approaches is the expectation that degrees of freedom in the respective transition metal coordination complex are reduced, resulting in the simulation of a preorganized bidentate system with predictable geometric properties, as in conventional bidentate ligands.

Studies aimed at the introduction of an additional phosphorus functionality in the salen moiety of the salen-cobalt(III)-*N*-benzyl-serine-derived phosphite ligands are currently underway to realize a new class of supramolecular bidentate ligands.

4. Experimental

4.1. General methods

All reactions were carried out in flame-dried glassware with magnetic stirring under a nitrogen atmosphere, unless otherwise stated. Commercially available dry solvents (over molecular sieves in bottles with crown cap) were stored under nitrogen and used without further distillation. TEA was distilled over CaH_2 under nitrogen. Reactions were monitored by analytical thin-layer chromatography (TLC) using Silica Gel 60 F_{254} precoated glass plates (0,25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with a permanganate alkaline solution. Flash chromatography was performed using Silica Gel 60 Å, particle size 40–64 μm, following the procedure by Still and co-workers.[13] ^{1}H NMR spectra were recorded on a spectrometer operating at 400.13 MHz. Proton chemical shifts are reported in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard ($CDCl_3$ 7.28 ppm). The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal, dd = doublet of doublet. ^{13}C NMR spectra were recorded on a 400 MHz spectrometer operating at 100.56 MHz, with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as internal standard ($CDCl_3$, 77.0 ppm). ^{31}P NMR spectra were recorded on a 400 MHz spectrometer operating at 162 MHz, with complete proton decoupling. ^{31}P NMR chemical shifts are reported in ppm (δ) relative to external 85% H_3PO_4 at 0 ppm (positive value downfield). Infrared spectra were recorded on a standard FT/IR spectrometer; bands are reported in cm^{-1}. Optical rotation values were measured on an automatic polarimeter with a 1 dm cell at the sodium D line (λ = 589 nm). HPLC analyses were performed with a chiral stationary phase column Chiralcel OD-H (eluent hexane/isopropanol 90:10, flow 0.6 mL/min, t_R = 35 min (first enantiomer) 44 min (second enantiomer), λ = 254 nm. High resolution mass spectra (HRMS) were performed on Fourier Transform Ion Cyclotron Resonance (FT-ICR), Mass Spectrometer APEX II, and Xmass software (Bruker Daltonics)-4.7 T Magnet (Magnex). Commercially available reagents were used as received. (*S*,*S*)-*N*,*N*′-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(III) acetate **1**,[3] *N*-benzyl-L-serine,[14] and diol-derived monochlorophosphites were synthesized as reported in the literature.[4]

4.2. Synthesis of (*S*,*S*) salen-Co(III)-*N*-Bn-L-serine complex 2

To a solution of the cobalt complex (*S*,*S*)-(salen)Co(III)(OAc) **1** (1.65 g, 2.38 mmol) in dichloromethane (300 mL) at rt in a 1 L round-bottomed flask, a solution of *N*-Bn-L-serine (464 mg, 1.0 equiv, 2.38 mmol) in H_2O (100 mL) was added. The biphasic mixture was stirred vigorously overnight at rt, and then transferred to a separating funnel. The organic phase was removed and the aqueous phase washed twice with dicholoromethane (40 mL). The combined organic phases were washed once with H_2O (40 mL), dried over Na_2SO_4, and the solvent removed under reduced pressure. The crude was purified by flash chromatography (dicholoromethane/methanol 95:5) to afford the product as a green powder (1.82 g, yield 96%). Mp decomposition at 160 °C. $[\alpha]_D^{22} = -1671.1$ (*c* 0.027, $CHCl_3$); IR (Nujol) ν_{max} 3346, 3215, 2730, 1638, 1644, 1615, 1524, 1377, 1256, 1168, 1015, 930, 781 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.92 (s, 1H), 7.44 (d, 1H, *J* = 2.4 Hz), 7.39 (s, 1H), 7.30 (d, 1H, *J* = 2.4 Hz), 7.26–7.19 (m, 4H),7.13 (d, 1H, *J* = 2.3), 6.62 (d, 2H, *J* = 7.0 Hz), 5.35 (m, 1H) 4.63(m, 2H), 4.02 (d, 1H, *J* = 13.6 Hz), 3.43–3.25 (m, 3H), 2.94 (m, 1H), 2.80 (m, 1H), 2.29 (m, 1H), 2.18 (m, 1H), 1.73–1.61 (m, 3H), 1.54 (s, 9H), 1.38 (s, 19 H), 1.18 (s, 9H), 1.0–0.94 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$) δ 163.7, 163.3, 162.6, 160.1, 144.3, 141.1, 137.3, 136.9, 134.4, 129.8, 129.2, 128.9, 128.2, 125.7, 122.6, 117.4, 75.2, 70.8, 62.7, 55.4, 35.8, 34.0, 33.8, 31.5, 31.4, 31.0, 29.7, 29.6, 25.1, 22.6 ppm. HRMS (ESI+) *m*/*z* calcd for $[C_{46}H_{64}CoNaN_3O_5]^+$: 820.40702 $[M+Na]^+$; found: 820.40507.

4.3. General procedure for the synthesis of the (*S*,*S*)-salen-Co(III)-*N*-Bn-L-serine complex phosphites 3a–3d

The (*S*,*S*)-salen-Co(III)-*N*-Bn-L-serine complex **2** (120 mg, 0.15 mmol) was dissolved in THF (1.0 mL) in a Schlenk under a nitrogen atmosphere. Freshly distilled TEA (42 μL, 0.3 mmol, 2 equiv) was added to the green solution at rt and the whole mixture was cooled to −78 °C. A solution of the diol-derived monochlorophosphite (0.18 mmol, 1.2 equiv) in THF (1.0 mL) was added dropwise and the reaction mixture was allowed to warm to rt. After 20 min the solvent was removed under reduced pressure and the crude was quickly purified by flash chromatography to afford the product as a green fine powder.

4.3.1. (*S,S*)-Salen-Co(III)-*N*-Bn-L-serine-biphenyl-phosphite 3a

(Hexane/AcOEt 3:2 R_f = 0.50) (76 mg, yield 50%). $[\alpha]_D^{23} = -681.8$ (*c* 0.094, $CHCl_3$). IR (Nujol) ν_{max} 3231, 2705, 1672, 1643, 1615, 1529, 1377, 1321, 1250, 1207, 1168, 1096, 1015, 897, 739 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.84 (s, 1H), 7.44–7.43 (m, 4H), 7.36–7.12 (m, 12H), 6.65 (d, 2H, *J* = 7.3 Hz), 5.16 (m, 1H), 4.66 (dd, 1H, *J* = 13.6 Hz, *J* = 3.8 Hz), 4.12 (dd, 1H, *J* = 5.9 Hz, *J* = 3.8 Hz), 4.02 (m, 2H), 3.46 (m, 1H), 2.98 (m, 1H), 2.82 (m, 1H), 2.71 (m, 1H), 1.96–1.55 (m, 4H), 1.55 (s, 10H), 1.42 (s, 9H), 1.36 (s, 10H), 1.17 (s, 10H) ppm. ^{13}C NMR ($CDCl_3$) δ 179.8, 164.9, 163.5, 163.4, 160.7, 150.1, 149.3, 144.9, 141.2, 137.7, 137.0, 135.2, 131.8, 130.4, 130.3, 130.1, 129.8, 129.7, 129.6, 129.4, 129.1, 128.8, 126.0, 125.7, 125.6, 122.8, 122.5, 122.4, 120.9, 118.1, 117.9, 75.9, 70.6, 65.5, 65.3, 64.89, 64.8, 55.9, 36.2, 34.5, 34.2, 32.0, 31.9, 31.1, 30.3, 29.9, 29.3, 25.0, 24.3 ppm. ^{31}P NMR ($CDCl_3$) δ 164.6 ppm. HRMS (ESI+) *m/z* calcd for $[C_{58}H_{71}CoNaN_3O_7P]^+$: 1034.42538 $[M+Na]^+$; found: 1034.42271. Decomposition by-product: ^1H NMR ($CDCl_3$) δ 8.30 (br s, 1H), 8.01 (br s, 1H), 7.51 (d, 1H, *J* = 2.4 Hz), 7.44 (d, 1H, *J* = 2.4 Hz), 7.32 (dd, 1H, *J* = 7.4 Hz, *J* = 1.3 Hz), 7.26 (d, 1H, *J* = 7.2 Hz), 7.21 (d, 1H, *J* = 2.4 Hz), 7.17 (d, 1H, *J* = 2.4 Hz), 7.13–7.04 (m, 2H), 6.99–6.95 (m, 1H), 6.68–6.64 (m, 1H), 6.14 (d, 1H, *J* = 7.7 Hz), 5.47 (d, 1H, *J* = 8.2 Hz), 4.25–4.18 (m, 1H), 3.73–3-67 (m, 1H), 2.91 (d, 1H, *J* = 10.5 Hz), 2.78 (d, 1H, *J* = 9.7 Hz), 2.09–2.05 (m, 2H), 1.96–1.87 (m, 1H), 1.78–1.68 (m, 1H), 1.63–1.49 (m, 2H), 1.48 (s, 9H), 1.43 (s, 9H), 1.40 (s, 9H), 1.22 (s, 9H) ppm. ^{31}P NMR ($CDCl_3$) δ 37.5 ppm.

4.3.2. (*S,S*)-Salen-Co(III)-*N*-Bn-L-serine-3,3′,5,5′-biphenyl-phosphite 3b

(Hexane/AcOEt 3:1 R_f = 0.40) (115 mg, yield 72%). $[\alpha]_D^{23} = -1050.8$ (*c* 0.077, $CHCl_3$); IR (Nujol) ν_{max} 3251, 3232, 2726, 1680, 1645, 1618, 1535, 1380, 1320, 1257, 1212, 1168, 1093, 1015, 860, 739 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.81 (s, 1H), 7.42 (d, 1H, *J* = 2.5 Hz), 7.38–7.28 (m, 4H), 7.27 (d, 1H, *J* = 2.4 Hz), 7.18 (s, 1H), 7.12–7.11 (m, 2H), 7.06 (s, 1H), 7.00 (d, 1H, *J* = 2.3 Hz), 6.75 (m, 2H), 6.51 (s, 1H), 5.04 (m, 1H), 4.68 (m, 1H), 4.34 (m, 1H), 4.15 (dd, 1H, *J* = 14.3 Hz, *J* = 7.13 Hz), 4.01–3.92 (m, 2H), 3.52 (m, 1H), 2.89–2.78 (m, 2H), 2.62–2.58 (m, 1H), 2.46 (s, 3H), 2.37 (s, 6H), 2.30 (s, 3H), 1.83–1.70 (m, 3H), 1.57 (s, 9H), 1.50 (s, 9H), 1.36 (s, 10H), 1.23–1.17 (m, 11H) ppm. ^{13}C NMR ($CDCl_3$) δ 179.3, 164.8, 163.5, 147.4, 145.0, 144.8, 141.2, 137.6, 135.6, 135.1, 134.8, 133.9, 132.1, 131.9, 131.3, 131.2, 130.7, 130.4, 130.2, 129.6, 129.5, 129.0, 128.4, 127.7, 126.0, 122.8, 118.2, 75.9, 71.0, 66.3, 66.1, 65.9, 60.8, 55.9, 36.1, 34.6, 34.1, 32.2, 31.9, 31.3, 30.3, 29.9, 29.5, 25.0, 23.9, 21.3, 17.4, 16.9, 14.6 ppm. ^{31}P NMR ($CDCl_3$) δ 150.7 ppm. HRMS (ESI+) *m/z* calcd for $[C_{62}H_{79}CoNaN_3O_7P]^+$: 1090.48798 $[M+Na]^+$; found: 1090.48576.

4.3.3. (*S,S*)-Salen-Co(III)-*N*-Bn-L-serine-(S_a)-binaphthyl-phosphite 3c

(Hexane/AcOEt 2:1 R_f = 0.40) (62 mg, yield 37%). $[\alpha]_D^{22} = -775.2$ (*c* 0.078, $CHCl_3$); IR (Nujol) ν_{max} 3159, 2722, 1660, 1634, 1615, 1526, 1365, 1321, 1255, 1230, 1168, 945, 828, 730 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.06 (d, 1H, *J* = 8.8 Hz), 7.97 (d, 1H, *J* = 8.3 Hz), 7.87 (d, 1H, *J* = 8.5 Hz), 7.82 (d, 1H, *J* = 8.8 Hz), 7.77 (m, 1H), 7.62 (d, 1H, *J* = 8.7 Hz), 7.50–7.33 (m, 9H), 7.31–7.26 (m, 3H), 7.13 (d, 1H, *J* = 8.7 Hz), 7.08–7.06 (m, 2H), 6.73 (m, 2H), 5.32 (m, 1H), 4.67 (m, 1H), 4.16–4.04 (m, 3H), 3.59 (m, 1H), 3.46 (m, 1H), 2.80 (m, 1H), 2.73–2.68 (m, 2H), 1.77–1.63 (m, 3H), 1.54 (s, 9H), 1.42 (s, 9H), 1.41–1.35 (m, 2H), 1.33 (s, 9H), 1.19–1.12 (m, 10H) ppm. ^{13}C NMR ($CDCl_3$) δ 179.2, 164.4, 163.1, 162.9, 160.7, 152.0, 147.7, 146.8, 144.5, 140.8, 137.3, 136.9, 134.8, 132.9, 132.1, 131.7, 131.0, 130.7, 130.5, 130.4, 130.2, 129.9, 129.8, 129.3, 128.6, 128.5, 128.4, 127.2, 127.0, 126.6, 126.5, 126.2, 125.7, 125.4, 124.9, 122.1, 122.0, 121.6, 119.3, 118.0, 117.7, 75.5, 69.7, 64.6, 64.5, 63.6, 63.5, 55.4, 35.8, 34.1, 33.7, 31.6, 31.4, 30.4, 30.1, 29.8, 29.5, 29.1, 28.5, 24.4, 23.6 ppm. ^{31}P NMR ($CDCl_3$) δ 146.6 ppm. HRMS (ESI+) *m/z* calcd for $[C_{66}H_{75}CoNaN_3O_7P]^+$: 1134.45668 $[M+Na]^+$; found: 1134.45474.

4.3.4. (*S,S*)-Salen-Co(III)-*N*-Bn-L-serine-(R_a)-binaphthyl-phosphite 3d

(Hexane/AcOEt 2:1 R_f = 0.40) (75 mg, yield 45%). $[\alpha]_D^{23} = -1227.3$ (*c* 0.055, $CHCl_3$); IR (Nujol) ν_{max} 3221, 2725, 1670, 1652, 1634, 1521, 1377, 1314, 1256, 1168, 1095, 1023, 945; 823, 744 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.06–7.59 (m, 3H), 7.80 (s, 1H), 7.59 (d, 1H, *J* = 8.7 Hz), 7.51–7.45 (m, 2H), 7.42–7.27 (m, 7H), 7.20 (d, 1H, *J* = 2.4 Hz), 7.09–6.96 (m, 5H), 6.59–6.57 (m, 3H), 4.85 (m, 1H), 4.59 (m, 1H), 4.17–4.09 (m, 2H), 3.91 (m, 1H), 3.42 (m, 1H), 2.88–2.75 (m, 2H), 2.61 (m, 1H), 1.99–1.85 (m, 3H), 1.56–1.41 (m, 19H), 1.36–1.34 (m, 10H), 1.28–1.25 (m, 1H), 1.22–1.12 (m, 11H) ppm. ^{13}C NMR ($CDCl_3$) δ 179.2, 164.4, 162.9, 161.2, 159.6, 148.3, 147.0, 144.4, 140.8, 137.1, 136.4, 134.8, 132.7, 132.3, 131.6, 130.8, 130.6, 129.9, 129.8, 129.3, 129.1, 129.0, 128.8, 128.4, 128.3, 126.9, 126.8, 126.4, 126.3, 126.0, 125.6, 125.2, 125.1, 124.5, 123.9, 123.5, 122.6, 75.5, 70.4, 66.3, 66.1, 65.1, 55.5, 35.7, 34.1, 33.7, 31.7, 31.4, 30.6, 29.8, 29.4, 29.0, 24.5, 23.7 ppm. ^{31}P NMR ($CDCl_3$) δ 144.2 ppm. HRMS (ESI+) *m/z* calcd for $[C_{66}H_{75}CoNaN_3O_7P]^+$: 1134.45668 $[M+Na]^+$; found: 1134.45423.

4.4. General procedure for the Pd-catalyzed desymmetrization of *meso*-cyclopenten-2-ene-1,4-diol biscarbamate[9]

To a solution of the *meso*-cyclopenten-2-ene-1,4-diol (10 mg, 0.099 mmol) in 0.5 mL of THF, tosyl isocyanate (35 μL, 0.232 mmol, 2.35 equiv) was added. The mixture was stirred at rt for 15 min to give a colorless solution and then heated to 55 °C for 1 h. The reaction was cooled back to rt, and triethylamine (14.0 μL, 0.099 mmol, 1.0 equiv) was added. The resulting white slurry was brought to the chosen temperature conditions and a solution of tris(dibenzylidine acetone)dipalladium(0) chloroform complex (5.1 mg, 4.94 μmol) and ligand (20.25 μmol) in 0.5 mL of THF was added (the solution of the Pd-source and the ligand was prepared under nitrogen and stirred for 40 min at rt, 10 min at 55 °C and finally cooled back to rt). The reaction solution was stirred for 30 min. The solvent was removed in vacuo and purified by flash chromatography on a short pad of silica gel (10 cm, hexane/AcOEt 80:20) gave the desired products as a slightly brown solid. Conversions were determined by NMR analysis of the crude reaction mixture. Enantiomeric excesses were determined by chiral HPLC (column Chiralcel OD-H, *n*-hexane/2-propanol 90:10, flow 0.6 ml/min).

Acknowledgments

We thank the European Commission [EST-project 'Foldamers' MEST-CT-2004-515968 and RTN Network (R)Evolutionary Catalysis MRTN-CT-2006-035866] for financial support. The Università degli Studi dell'Insubria is gratefully acknowledged for a post-doctoral fellowship (assegno di ricerca) to L.P. C.G. thanks Merck Research Laboratories for the Merck's Academic Development Program Award.

References

1. Larrow, J. R.; Jacobsen, E. N. *Top. Organomet. Chem.* **2004**, *6*, 123–152. and references therein.
2. (a) Reeve, T. B.; Cros, J.-P.; Gennari, C.; Piarulli, U.; de Vries, J. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 2449–2453; (b) Dzygiel, P.; Reeve, T. B.; Piarulli, U.; Krupicka, M.; Tvaroska, I.; Gennari, C. *Eur. J. Org. Chem.* **2008**, 1253–1264; For the extension of this method to the resolution of racemic *N*-benzyl β^3-amino acids, see: (c) Dzygiel, P.; Monti, C.; Piarulli, U.; Gennari, C. *Org. Biomol. Chem.* **2007**, *5*, 3464–3471.
3. Nielsen, P. C. L.; Stevenson, P. C.; Blackmond, D. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 1360–1362.

4. For the synthesis of the diol derived chlorophosphites see: Franciò, G.; Arena, C. G.; Faraone, F.; Graiff, C.; Lanfranchi, M.; Tiripicchio, A. *Eur. J. Inorg. Chem.* **1999**, 1219–1227.
5. Reetz, M. T.; Bondarev, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 4523–4526. and references therein.
6. Diéguez, M.; Pàmies, O.; Claver, C. *J. Org. Chem.* **2005**, *70*, 3363–3368.
7. Ruffo, F.; Del Litto, R.; De Roma, A.; D'Errico, A.; Magnolia, S. *Tetrahedron: Asymmetry* **2006**, *17*, 2265–2269.
8. (a) Graening, T.; Schmalz, H.-G. *Angew. Chem., Int. Ed.* **2003**, *42*, 2580–2584; (b) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2943.
9. Trost, B. M.; Patterson, D. E. *J. Org. Chem.* **1998**, *63*, 1338–1341.
10. (a) Reetz, M. T. *Angew. Chem., Int. Ed.* **2008**, *47*, 2556–2588. and references therein; (b) Sandee, A. J.; Reek, J. N. H. *Dalton Trans.* **2006**, 3385–3391; (c) Breit, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 6816–6825.
11. Goudriaan, P. E.; Jang, X.-B.; Kuil, M.; Lemmens, R.; Van Leeuwen, P. W. N. M.; Reek, J. N. H. *Eur. J. Org. Chem.* **2008**, 6079–6092. and references therein.
12. Moteki, S. A.; Takacs, J. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 894–897. and references therein.
13. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
14. Quitt, P.; Hellerbach, J.; Vogler, K. *Helv. Chim. Acta* **1963**, *46*, 327–333.